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## Osteogenic activity of the fourteen types of human bone morphogenetic proteins (BMPs).

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**BACKGROUND:** Bone morphogenic proteins (BMPs) are known to promote osteogenesis, and clinical trials are currently underway to evaluate the ability of certain BMPs to promote fracture-healing and spinal fusion. The optimal BMPs to be used in different clinical applications have not been elucidated, and a comprehensive evaluation of the relative osteogenic activity of different BMPs is lacking. **METHODS:** To identify the BMPs that may possess the most osteoinductive activity, we analyzed the osteogenic activity of BMPs in mesenchymal progenitor and osteoblastic cells. Recombinant adenoviruses expressing fourteen human BMPs (BMP-2 to BMP-15) were constructed to infect pluripotent mesenchymal progenitor C3H10T1/2 cells, preosteoblastic C2C12 cells, and osteoblastic TE-85 cells. Osteogenic activity was determined by measuring the induction of alkaline phosphatase, osteocalcin, and matrix mineralization upon BMP stimulation. **RESULTS:** BMP-2, 6, and 9 significantly induced alkaline phosphatase activity in pluripotential C3H10T1/2 cells, while BMP-2, 4, 6, 7, and 9 significantly induced alkaline phosphatase activity in preosteoblastic C2C12 cells. In TE-85 osteoblastic cells, most BMPs (except BMP-3 and 12) were able to induce alkaline phosphatase activity. The results of alkaline phosphatase histochemical staining assays were consistent with those of alkaline phosphatase colorimetric assays. Furthermore, BMP-2, 6, and 9 (as well as BMP-4 and, to a lesser extent, BMP-7) significantly induced osteocalcin expression in C3H10T1/2 cells. In C2C12 cells, osteocalcin expression was strongly induced by BMP-2, 4, 6, 7, and 9. Mineralized nodules were readily detected in C3H10T1/2 cells infected with BMP-2, 6, and 9 (and, to a lesser extent, those infected with BMP-4 and 7). **CONCLUSIONS:** A comprehensive analysis of the osteogenic activity of fourteen types of BMPs in osteoblastic progenitor cells was conducted. Our results suggest an osteogenic hierarchical model in which BMP-2, 6, and 9 may play an important role in inducing osteoblast differentiation of mesenchymal stem cells. In contrast, most BMPs are able to stimulate osteogenesis in mature osteoblasts.

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